A randomized, subject and investigator-blind, placebo-controlled study of CLR325 in chronic stable heart failure patients.

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To determine the safety, tolerability and pharmacokinetics of an 18-hour i.v. infusion of CLR325 in stable heart failure patients.

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Heart failures
Study type	Interventional

Summary

ID

NL-OMON46128

Source
ToetsingOnline

Brief title
CCLR325X2202

Condition

- Heart failures

Synonym
heart failure

Research involving
Human

Sponsors and support

Primary sponsor: Novartis
Source(s) of monetary or material Support: Novartis Pharma B.V. (sponsor/verrichter

van dit onderzoek)

Intervention

Keyword: Apelin, chronic heartfailure, CLR325

Outcome measures

Primary outcome

To determine the safety and tolerability of an 18-hour IV infusion of CLR325 in stable heart failure patients.

Secondary outcome

To determine the pharmacokinetics of CLR325, and the active metabolite, CQJ295, during an 18-hour infusion of CLR325 in heart failure patients. To determine the immunogenicity of an 18-hour i.v. infusion of CLR325 in heart failure patients.

Study description

Background summary

Acute decompensated heart failure is commonly caused by deteriorating cardiac function that leads to unplanned, often urgent, medical intervention. There are ~ 500,000 hospitalizations annually for acute decompensated heart failure in the USA and the 30-day mortality following hospitalization is up to 11% (Jong et al 2002). Intravenous inotropes, including dobutamine (*-agonist), and milrinone/amrinone (PDEIII inhibitors) are used to augment cardiac output in these patients and are associated with increased risk of arrhythmia and mortality (Felker and O'Connor 2001). In contrast, digoxin does not increase all-cause mortality, and reduces heart failure hospitalizations in patients with heart failure (Digitalis Investigation 1997), but it is a weak inotrope with a narrow therapeutic index. Therefore, new inotropic therapies that can effectively enhance cardiac function without increasing the risk of arrhythmias and/or mortality are urgently needed for patients with heart failure.

Study objective

To determine the safety, tolerability and pharmacokinetics of an 18-hour i.v. infusion of CLR325 in stable heart failure patients.

Study design

This is a randomized, double-blind, placebo-controlled study with an administration of CLR325 for 18 hours to assess safety, tolerability and pharmacokinetics in patients with stable heart failure.
The study is made up of 4 cohorts, in which cohort 1 and 2 the required patients have now been found.
For the participating Dutch center, only the PA cohort will apply, since the echo cohort will be full by the end of this month.
The study consists of a screening visit (up to 45 days prior to randomization), baseline period + treatment period (28 hours) and a follow-up period (up to 28 days). The treatment period will be 1 hour prior to treatment, treatment (18 h) and a period after treatment (10 h).
The patients will be asked to return to the study site on Day 10 for a follow-up visit and on Day 28 for an end-of-study visit.

Intervention

Infusion of 18 hours with CLR325 (8 ug/kg/min) or Placebo (NaCL 0,9%)

Study burden and risks

Risk:
Adverse effects of study medication (CLR326) and study procedures.

Burden:
- Physical examination: 5x
- Vital signs: 5x
- Weight measurements:5x
- Collection of blood samples: 16x
- ECG: 10x
- Urine collection: 5x
- 24-hour urine collection: 1x
- Cardiac haemodynamic monitoring/telemonitoring: 2x

Contacts

Public
Novartis

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Scientific
Novartis

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

- Written informed consent must be obtained before any assessment is performed;
- Able to communicate well with the investigator, to understand and comply with the requirements of the study;
- Male and female patients >18 years of age.
- Patients must weigh between 50kg and 140 kg to participate in the study;
- Patients with a cardiac ejection fraction of * 45% as assessed within the last 6 months;
- For PA catheter cohorts, patients who are planned to have a clinically indicated pulmonary artery catheter in place prior to randomization;
- In the opinion of the investigator, heart failure patients who will not require a change in their dose of ACE, ARB, *-blocker, mineralocorticoid receptor antagonist, or diuretic for 24 hours after randomization
- At baseline, vital signs (systolic and diastolic blood pressure and pulse rate) will be assessed in the sitting position after the subject has rested for at least five minutes

Exclusion criteria

- Presence of impaired renal function as indicated by clinically significant abnormal creatinine values (eGFR< 30 ml/min/1.73m2 calculated using the MDRD equation)

- Patients with values of AST or ALT>100 U/L measured within the last 3 months before randomization
- Chronic infection with Hepatitis B (HBV) or Hepatitis C (HCV). positive Hepatitis B surface antigen (HBsAg) test excludes a patient. Patients with a positive Hepatitis C antibody test should have HCV RNA levels measured. Patients with positive (detectable) HCV RNA should be excluded.
- Patients with a history of chronic hepatitis of any non-cardiac etiology.
- History of any active, clinically significant cardiac tachyarrhythmia, such as recurrent atrial fibrillation with rapid ventricular response within the last year. Anticoagulation for patients with atrial fibrillation should be managed per usual clinical practice for patients undergoing right heart catheterization.
- Patients who have received an intravenous infusion of a cardiac inotrope (e.g.,dobutamine or milrinone) in the last 24 hours prior to randomization.
- For PA catheter cohorts, patients with a pulmonary capillary wedge pressure of >10 mm Hg at baseline.
- Patients with any significant change in their dose of their ACE, ARB, mineralocorticoid receptor antagonist, diuretic or *-blocker within the last 12 hours.
- Patients with minor changes in their heart failure regimen may be eligible if deemed clinically stable by both the investigator and sponsor.
- Patients with known significant valvular heart disease, as indicated by the following:
- Severe aortic stenosis (Aortic Valve Area >1.0 cm2 or peak gradient 50 mmHg as determined by echocardiography)
- Severe mitral stenosis
- Patients with history of acute coronary syndrome within the last 60 days as determined by both clinical and enzymatic criteria.

Study design

Design

Study phase:	2
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	11-10-2018
Enrollment:	2
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	CLR325
Generic name:	CLR325

Ethics review

Approved WMO Date:	08-08-2018
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	25-09-2018
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	26-09-2018
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	22-01-2019
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	20-02-2019
Application type:	Amendment
Review commission:	METC Amsterdam UMC

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
EudraCT	EUCTR2016-001387-12-NL
ClinicalTrials.gov	NCT02696967
CCMO	NL66601.029.18